REMARKS

Claims 1, 7-10, 12-16, 25, and 28-47 presently appear in this application and a clean copy of all pending claims is attached hereto. Original claims 1-46 are subject to a restriction requirement. None of the claims have yet been acted upon on the merits. The Office Action of November 5, 2002, has now been carefully studied. Reconsideration and withdrawal of the restriction requirement and action on all of claims 1, 7-10, 12-16, 25, and 28-47, are hereby respectfully solicited.

The examiner indicates that the claims are directed to four separate patentably distinct inventions and requires restriction to one of the following:

Group I, claims 1-18, drawn to an isolated DNA molecule comprising a kidney specific promoter operably linked to a heterologous DNA sequence containing a non-native apical surface membrane targeting sequence;

Group II, claims 19-28 drawn to a transgenic non-human mammal and a method of producing a recombinant polypeptide using the non-human mammal, wherein the germ and somatic cells of the non-human mammal contain a recombinant construct comprising a kidney specific promoter operably linked to a heterologous DNA sequence containing a non-native apical surface membrane targeting sequence;

Group III, claims 29-37, drawn to an isolated DNA molecule comprising a kidney specific promoter operably linked to a heterologous DNA sequence in which basolateral surface membrane targeting signals are inactivated or deleted; and

Group IV, claims 38-46, drawn to a transgenic non-human mammal and a method of producing a recombinant polypeptide using the non-human mammal, wherein the germ and somatic cells of non-human mammal contain a recombinant construct comprising a kidney specific promoter operably linked to a heterologous DNA sequence in which basolateral surface membrane targeting signals are inactivated or deleted.

Applicants provisionally elect Group I, drawn to an isolated DNA molecule comprising a kidney-specific promoter operably linked to a heterologous DNA sequence containing a non-native apical surface membrane targeting sequence and presently comprising claims 1, 7-10, and 12-16 with traverse.

Traversal of restriction between Groups I and III is based on the amendment to the claims to rewrite claim 29 to be generic by reciting the feature of a kidney-specific promoter operably linked to a heterologous DNA sequence without requiring either the presence of a non-native apical surface membrane targeting sequence or the inactivation or deletion of any basolateral surface membrane targeting signals. Accordingly, Groups I (claims 1, 7-10, and 12-16) and III (new claim 47) are merely different embodiments of the present invention as defined by generic claim 29. Claim 29 as amended is fully supported by the present specification at page 9, lines 14-20, and parent application 09/438,785, the entire contents of which have been incorporated by reference into the instant application.

The claims as amended eliminates the distinction between Groups II and IV. Applicants were recently granted a U.S. Patent

6,339,183, a copy of which is attached hereto, directed to a bladder bioreactor system with claims to a DNA construct, a non-human transgenic mammalian animal, and a method for producing a biologically active molecule in the urine of a non-human mammalian animal. Accordingly, applicants believe that claims to a kidney bioreactor system in the instant application, which includes claims to a DNA construct, a transgenic non-human mammal, and a method for producing a recombinant biologically active molecule in the urine, should all be examined together.

Withdrawal of the restriction requirement and examination of all the claims now present in the case are respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1 and 29 have been amended as follows below:

1(Once-amended). An isolated DNA molecule according to claim 29, wherein said heterologous polypeptide contains a non-native apical surface membrane targeting sequence~~, comprising a kidney-specific promoter operably linked to a heterologous DNA sequence encoding a heterologous polypeptide containing a non-native apical surface membrane targeting sequence, wherein said kidney-specific promoter is capable of driving the expression of said heterologous polypeptide *in vivo* in the kidneys to produce a recombinant biologically active polypeptide in the urine~~.

29(Once-amended). An isolated DNA molecule, comprising a kidney-specific promoter operably linked to a heterologous DNA sequence encoding a heterologous polypeptide, wherein said kidney-specific promoter directs expression of said heterologous polypeptide *in vivo* in the kidneys to produce a recombinant biologically active polypeptide in the urine~~ in which basolateral surface membrane targeting signals are inactivated or deleted~~.